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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,163	02/20/2002	Susanna Chubinskaya	STK-081	8382

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TESTA, HURWITZ & THIBEAULT, LLP
HIGH STREET TOWER
125 HIGH STREET
BOSTON, MA 02110

EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,163	CHUBINSKAYA ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 20, 2002*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-47* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). In the instant application there exits two claims numbered 23. Therefore the claims have been renumbered.

Misnumbered claims 1-46 been renumbered 1-47.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 5-8, 33, 34 and 43 drawn to a method of determining the presence of an inflammatory disease in a patient, classified in class 435, subclass 7.1.

II. Claims 2, 5, 6, 8, 33, 34 and 43, drawn to a method of determining the presence of an inflammatory disease, classified in class 435, subclass 6.

III. Claims 3, 5-8 and 43, drawn to a method for determining the clinical severity of an inflammatory disease in a patient, classified in class 435, subclass 7.92.

IV. Claims 4-6, 8 and 43, drawn to a method of determining the clinical severity of an inflammatory disease, classified in class 436, subclass 501.

V. Claims 9, 17-21, 23, 33, 34 and 44, drawn to a method of determining the presence of an age-related tissue disorder in a patient, classified in class 435, subclass 967.

VI. Claims 10, 17, 18, 20, 21, 23, 33, 34 and 44, drawn to a method of determining the presence of an age-related tissue disorder in a patient, classified in class 435, subclass 91.2.

VII. Claims 11, 17-19, 22, 23, 33 and 34, drawn to a method of determining the presence of a disorder characterized by accelerated or abnormal tissue aging in a patient, classified in class 435, subclass 7.93.

VIII. Claims 12, 17, 18, 22, 23, 33 and 34, drawn to a method of determining the presence of a disorder characterized by accelerated or abnormal tissue aging in a patient, classified in class 436, subclass 501.

IX. Claims 13, 17-21 and 44, drawn to a method for determining the clinical severity of an age-related tissue dosorder in a patient, classified in class 435, subclass 7.9.

X. Claims 14, 17, 18, 20, 21 and 44 drawn to a method for determining the clinical severity of an age-related tissue disorder in a patient, classified in class 435, subclass 6.

XI. Claim 15, drawn to a method for determining the clinical severity of a disorder characterized by accelerated or abnormal tissue aging in a patient, classified in class 436, subclass 86.

XII. Claim 16, drawn to a methodfor determining the clinical severity of a disorder characterized by abnormal tissue aging in a patient, classified in class 435, subclass 40.52.

XIII. Claims 24, 28-34 and 45, drawn to a method of determining the presence of an autoimmune disease in a patient, classified in class 436, subclass 506.

XIV. Claims 25, 28-30, 32-34 and 45, drawn to a method of determining the presence of an autoimmune disease in a patient, classified in class 436, subclass 811.

XV. Claims 26, 28-32 and 45, drawn to a method for determining the clinical severity of an autoimmune disease in a patient, classified in class 435, subclass 7.94.

XVI. Claims 27-30, 32 and 45, drawn to a method of determining the clinical severity of an autoimmune disease in a patient, classified in class 435, subclass 6.

XVII. Claim 35, drawn to a method of determining a predisposition for a disease which results in cartilage degradation or degeneration in a patient, classified in class 436, subclass 501.

XVIII. Claims 36-38, drawn to a method of determining a predisposition for a disease which results in cartilage degradation or degeneration in a patient, classified in class 435, subclass 7.1.

XIX. Claim 39, drawn to a method of monitoring regenerative or degenerative activity within a joint region of a patient, classified in class 435, subclass 4.

XX. Claim 40, drawn to a method of determining the clinical status of a joint region of a patient, classified in class 435, subclass 6.

XXI. Claim 41, drawn to a method for determining the effective dose of an anti-inflammatory agent in a subject , classified in class 435, subclass 7.2.

XXII. Claim 42, drawn to a method for determining the ability of a patient to respond to an anti-inflammatory agent, classified in class 424, subclass 78.05.

XXIII. Claim 46, drawn to a method of determining joint tissue deterioration, classified in class 435, subclass 91.51.

XXIV. Claim 47, drawn to a method of determining joint tissue aging,, classified in class 435, subclass 6.

2. Inventions I and II, IV, VI, VIII, X, XII, XIV, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and further Invention I involves determining OP-1 protein present whereas Inventions II, IV, VI, VIII, X, XII, XIV, XVI involve determining OP-1 mRNA.

3. Inventions I and III and XI are independent and distinct inventions. Invention I is a method of determining the presence of an inflammatory disease whereas Invention III is a method of determining the clinical severity of an inflammatory disease. Invention XI is a method for determining the clinical severity of a disorder characterized by accelerated or abnormal tissue aging in a patient. Invention I requires comparing the

amount of OP-1 present with a predetermined standard whereas Invention III and XI require applying the amount of a predetermined statistical relationship, the statistical relationship correlating a range of amount of OP-1 present in joint tissue samples obtained from members of a population having the inflammatory disease and Invention I does not require this limitation.

4. Inventions I and V, VII, IX, XIII, XV are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions differ in patient subpopulations. For example, for a method for determining inflammatory disease, one would have to study a population of patients having the inflammatory disease, for a method determining the presence of an age-related tissue disorder, one would have to study a specific age of patients. For a method of determining autoimmune disease, one would study persons with autoimmune disease.

5. Inventions I and XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention I is a method of determining the presence of an inflammatory disease in a patient whereas Invention XVII is a method of determining a predisposition for a disease which results in cartilage degradation or degeneration in a patient. Invention XVIII is a method of determining the clinical status of a joint region of a patient. Invention XX is a method of determining the clinical status of a joint region of a patient. Further, the methods would have different subpopulations of patients.

6. Inventions I-XVIII, XX-XXIV and XIX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, Invention XIX determining the relative amount of OP-1 protein present in at least one tissue sample obtained from the joint region of the patient, wherein the at least one said tissue sample corresponds to a point in time which is later than a first, earlier tissue sample for which OP-1 protein amounts are already determined and Inventions I-XVIII, and XX-XXIV do not require this limitation.

7. Inventions I-XX, XXIII, XXIV and XXII, XXIII are independent and distinct inventions. Invention I is a method of determining the presence of an inflammatory disease in a patient whereas Invention XXI is a method for determining the effective dose of an anti-inflammatory agent in a subject and Invention XXII is a method for determining the ability of a patient to respond to an anti-inflammatory agent. Inventions XXI and XXII require obtaining a tissue, body fluid or cell sample from a subject to whom a dose of an anti-inflammatory agent is earlier administered and Invention I does not require this limitation.

8. Inventions I-XXII and XXIII, XXIV are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Inventions XXIII and XXIV require determining an amount of bone morphogenic protein related to OP-1 or an amount of mRNA encoding a protein related to OP-1 and Inventions I-XXII do not require this limitation.

9. Inventions II and III, V, VII, IX, XI, XIII, XV, are independent and distinct inventions. The inventions are not disclosed as capable of use together and further

Invention II involves determining OP-1 mRNA present whereas inventions III, V, VII, IX, XI, XIII, and XV involve determining OP-1 protein present.

10. Inventions II and IV, X, XII are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention II require comparing the amount of OP-1 mRNA present with a predetermined standard whereas Inventions IV, X and XII require applying to the amount a predetermined statistical relationship.

11. Inventions II and VI, VIII, XIV, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions differ in patient subpopulations. For example, for a method for determining inflammatory disease, one would have to study a population of patients having the inflammatory disease, for a method determining the presence of an age-related tissue disorder, one would have to study a specific age of patients. For a method of determining autoimmune disease, one would study persons with autoimmune disease.

12. Inventions II and XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention II is a method of determining the presence of an inflammatory disease in a patient whereas Invention XVII is a method of determining a predisposition for a disease which results in cartilage degradation or degeneration in a patient. Invention XVIII is a method of determining the clinical status of a joint region of a patient. Invention XX is a

method of determining the clinical status of a joint region of a patient. Further, the methods would have different subpopulations of patients.

13. Inventions III and IV, VI, VIII, X, XII, XIV, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and further Invention IIII involves determining OP-1 protein present whereas Inventions IV, VI, VIII, X, XII, XIV, XVI involve determining OP-1 mRNA.

14. Inventions III and V, VII, XIII, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, Invention III requires applying to the amount a predetermined statistical relationship and Inventions V, VII, XIII, XVII, XVIII and XX do not require this limitation.

15. Inventions III and IX, XI, XV are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions differ in patient subpopulations. For example, for a method for determining inflammatory disease, one would have to study a population of patients having the inflammatory disease, for a method determining the presence of an age-related tissue disorder, one would have to study a specific age of patients. For a method of determining autoimmune disease, one would study persons with autoimmune disease.

16. Inventions IV and V, VII, IX, XI, XIII, XV are independent and distinct inventions. The inventions are not disclosed as capable of use together and further Invention IV

involves determining OP-1 mRNA present whereas inventions V, VII, IX, XI, XIII, and XV involve determining OP-1 protein present.

17. Inventions IV and VI, VIII, XIV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, Invention III requires applying to the amount a predetermined statistical relationship and Inventions VI, VIII, XIV, XVII, XVIII, XX do not require this limitation.

18. Inventions IV and X, XII, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions differ in patient subpopulations. For example, for a method for determining inflammatory disease, one would have to study a population of patients having the inflammatory disease, for a method determining the presence of an age-related tissue disorder, one would have to study a specific age of patients. For a method of determining autoimmune disease, one would study persons with autoimmune disease.

19. Inventions V and VI, VIII, X, XII, XIV, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and further Invention V involves determining OP-1 protein present whereas Inventions VI, VIII, X, XII, XIV, XVI involve determining OP-1 mRNA.

20. Inventions V and VII, XIII, XV, XVII, XVIII and XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention V is a method of determining the presence of an age-related

tissue disorder in a patient. Invention VII is a method of determining the presence of a disorder characterized by accelerated or abnormal tissue aging in a patient. Invention XIII is a method of determining the presence of an autoimmune disease in a patient. Invention XV a method for determining the clinical severity of an autoimmune disease in a patient Invention XVII is a method of determining a predisposition for a disease which results in cartilage degradation or degeneration in a patient. Invention XVIII is a method of determining the clinical status of a joint region of a patient. Further, the methods would have different subpopulations of patients.

21. Inventions V and IX, XI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Inventions IX and XI involve applying to the amount a predetermined statistical relationship and Invention V does not require this limitation.

22. Inventions VI and VII, IX, XI, XIII, XV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention VI involves determining OP-1 mRNA present whereas inventions VII, IX, XI, XIII, XV, XVII, XVIII and XX involve determining OP-1 protein present.

23. Inventions VI and VIII, XIV are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions require different subpopulations

24. Inventions VI and X, XII, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects.

Further, Invention VI involves comparing the amount of OP-1 mRNA with a predetermined standard whereas, Inventions X, XII, and XVI involves applying to the amount a predetermined statistical relationship which invention VI does not involve.

25. Inventions VII and VIII, X, XII, XIV, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention VII involves determining OP-1 protein present whereas Inventions VIII, X, II, XIV, XVI involve determining OP-1 mRNA.

26. Inventions VII and IX, XI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention VII involves comparing the amount of OP-1 protein with a predetermined standard whereas, Inventions IX and XI involve applying to the amount a predetermined statistical relationship.

27. Inventions VII and XIII, XV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions require different subpopulations.

28. Inventions VIII and IX, XI, XIII, XV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention VIII involves determining OP-1 mRNA present whereas inventions IX, XI, XIII, XV, XVII, XVIII and XX involve determining OP-1 protein present.

29. Inventions VIII and X, XII, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention VIII involves comparing the amount of OP-1 mRNA present with a

predetermined standard whereas, Inventions X, XII and XVI involves applying to the amount a predetermined statistical relationship and Invention VIII does not require this limitation.

30. Inventions VIII and XIV are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention VIII is a method of determining the presence of a disorder characterized by accelerated or abnormal tissue aging in a patient whereas, Invention XIV is a method of determining the presence of an autoimmune disease in a patient.

31. Inventions IX and X, XII, XIV, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention IX involves determining OP-1 protein present whereas Inventions X, XII, XIV, XVI involve determining OP-1 mRNA.

32. Inventions IX and XI, XV are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions require different subpopulations.

33. Inventions IX and XIII, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, Invention IX involves applying to the amount a predetermined statistical relationship whereas, Inventions XIII, XVII, XVIII, and XX involves comparing the amount of OP-1 protein with a predetermined standard.

34. Inventions X and XI, XIII, XV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have

different effects. Invention X involves determining OP-1 mRNA present whereas inventions XI, XIII, XV, XVII, XVIII and XX involve determining OP-1 protein present.

35. Inventions X and XII, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions require different subpopulations.

36. Inventions X and XIV are independent and distinct inventions. The inventions are not discloses as capable of use together and have different effects. Invention X involves applying to the amount a predetermined statistical relationship and Invention XIV involves comparing the amount of OP-1 mRNA with a predetermined standard.

37. Inventions XI and XII, XIV, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention XI involves determining OP-1 protein present whereas Inventions XII, XIV, XVI involve determining OP-1 mRNA.

38. Inventions XI and XIII, XV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, Invention XI involves applying to the amount a predetermined statistical relationship whereas, inventions XIII, XV, XVII, XVIII and XX involve comparing the amount of OP-1 protein present with a predetermined standard.

39. Inventions XII and XIII, XV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Invention XII involves determining OP-1 mRNA whereas Inventions XIII, XV, XVII, XVIII and XX involve determining OP-1 protein.

40. Inventions XII and XIV are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effect. Further, Invention XII involves applying to the amount a predetermined statistical relationship whereas, inventions XIV involves comparing the amount of OP-1 protein present with a predetermined standard.

41. Inventions XII and XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions require different subpopulations of patients.

42. Inventions XIII and XIV, XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, Invention XIII involves determining OP-1 protein whereas inventions XIV and XVI involve determining OP-1 mRNA.

43. Inventions XIII and XV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, the inventions require different subpopulations of patients.

44. Inventions XIV and XV, XVII, XVIII, XX are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, Inventions XIV involves determining OP-1 mRNA whereas inventions XV, XVII, XVIII and XX involves determining OP-1 protein.

45. Inventions XIV and XVI are independent and distinct inventions. The inventions are not disclosed as capable of use together and have different effects. Further, Invention XIV requires comparing the amount of OP-1 mRNA with a predetermined

standard whereas Invention XVI requires applying to the amount a predetermined statistical relationship.

46. Inventions XV and XVI are independent and distinct inventions. The inventions have not been disclosed as capable of use together and have different effects. Further, Invention XV involves determining OP-1 protein present whereas invention XVI involves determining OP-1 mRNA.

47. Inventions XV and XVII, XVIII, XX are independent and distinct inventions. The inventions have not been disclosed as capable of use together and have different effects. Further, the inventions require different subpopulations of patients.

48. Inventions XVI and XVII, XVIII, XX are independent and distinct inventions. The inventions have not been disclosed as capable of use together and have different effects. Further, Invention XVI involves determining OP-1 mRNA whereas Inventions XVII, XVIII and XX involve determining O-1 protein.

49. Inventions XVII - XVIII, XX are independent and distinct invention. The inventions are not disclosed as capable of use together and have different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and the search required for one group is not required for other restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

50. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
September 27, 2004

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
09/27/04